

CLAIMS

1. A method for obtaining a nucleic acid sequence comprising a (poly)peptide coding sequence, which increases the expression yield of a periplasmic protein in functional form in bacteria upon co-expression of said periplasmic protein and said (poly)peptide, comprising the steps of:
 - (a) providing a collection of host cells wherein each cell contains
 - (i) a first nucleic acid sequence out of a collection of nucleic acid sequences, and
 - (ii) a second nucleic acid sequence encoding said periplasmic protein;
 - (b) causing or allowing expression of
 - (i) (poly)peptides expressible from said collection of nucleic acid sequences, and
 - (ii) said periplasmic protein expressible from said second nucleic acid sequence;
 - (c) screening or selecting for a host cell expressing said periplasmic protein with increased functional yield;
 - (d) optionally, repeating step (c) one or more times;
 - (e) obtaining said first nucleic acid sequence contained in said host cell.
2. The method of claim 1, further comprising the step of identifying a (poly)peptide coding sequence comprised in said first nucleic acid sequence.
3. The method of claims 1 or 2, wherein said first nucleic acid sequence is or is derived from genomic DNA or mRNA of an organism, or cDNA.
4. The method of anyone of claims 1 to 3, wherein said first nucleic acid sequence comprises an at least partially randomized sequence.
5. The method of anyone of claims 1 to 4, wherein
 - (a) said first nucleic acid sequence is comprised in a vector which can be packaged in a filamentous phage particle, and

- (b) said periplasmic protein is a fusion protein of at least part of a filamentous phage coat protein and a further protein;
and wherein in the course of said expression a collection of filamentous phage particles displaying said further protein is produced from said collection of host cells.
6. The method of anyone of claims 1 to 5 wherein said further protein comprises at least a domain of the immunoglobulin superfamily, and preferably of the immunoglobulin family.
 7. The method of claim 6 wherein said further protein is an immunoglobulin fragment taken from the list of Fv, scFv, disulphide-linked Fv, and Fab fragments.
 8. A method for identifying a (poly)peptide which increases the expression yield of a periplasmic protein in functional form in bacteria upon co-expression of said periplasmic protein and said (poly)peptide, comprising the steps of:
 - (a) identifying a nucleic acid sequence or a (poly)peptide coding sequence according to a method of anyone of claims 1 to 7, and
 - (b) deducing a (poly)peptide therefrom.
 9. A method for increasing the expression of a periplasmic protein in functional form in a bacterial host cell, characterized by co-expressing said periplasmic protein and a (poly)peptide identified by the method according to claim 8.
 10. The method of claim 9, wherein said periplasmic protein is a member of a collection of periplasmic proteins expressed in a collection of host cells.
 11. The method of claims 9 or 10 wherein said (poly)peptide is the *E. coli* protein Skp or a homolog thereof.

12. The method of claims 9 or 10 wherein said (poly)peptide is the *E. coli* protein FkpA or a homolog thereof.
13. The method of anyone of claims 9 to 12 wherein said periplasmic protein ia a fusion protein of at least part of a filamentous phage coat protein and a further protein.
14. The method of anyone of claims 9 to 13 wherein said further protein comprises at least a domain of the immunoglobulin superfamily, and preferably of the immunoglobulin family.
15. The method of claim 14, wherein the further protein is an immunoglobulin fragment taken from the list of Fv, scFv, disulphide-linked Fv, and Fab fragment.